

Diagnostic Accuracy of Drop Hydrogen Peroxide Test as a Novel Bedside Diagnostic Test to Differentiate Transudative and Exudative Pleural Effusion Against Light's Criteria

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ABSTRACT

Background

Diagnostic evaluation of pleural fluid according to Light's criteria to differentiate between exudative and transudative fluid takes 1 or 2 working days. For rapid clinical management, especially in critically ill patients, a simpler bedside diagnostic test can be done which has similar diagnostic accuracy as that of Light's Criteria.

Objective

To determine the diagnostic accuracy of Drop Hydrogen Peroxide test to differentiate exudative and transudative pleural effusion in comparison to Light's criteria.

Method

A concurrent validity test was performed using a convenient sampling technique including patients presenting to the Department of Internal Medicine from January to September 2021, who had pleural effusion. Two milliliters of tapped pleural fluid of patients who underwent aseptic thoracentesis was collected in a test tube to which one to two drops of 20% hydrogen peroxide was added. Presence of bubbles suggested an exudative type of fluid. Rest of the tapped pleural fluid was sent to the laboratory for further evaluation by Light's criteria, which was compared with the results by Drop Hydrogen Peroxide Test.

Result

There were 83 patients who had pleural effusion, of them a total of 43 patients had transudative pleural effusion while 40 patients had exudative pleural effusion based on Light's criteria and 37 patients had transudative pleural effusion while 46 patients had exudative pleural effusion based on drop hydrogen peroxide test.

Conclusion

The drop hydrogen peroxide test allows cost effective and prompt evaluation of the type of pleural effusion is exudative or transudative, thereby making it a convenient diagnostic bedside test.

KEY WORDS

Diagnostic tests, Exudates and Transudates, Hydrogen peroxide, Pleural effusion, Thoracentesis

INTRODUCTION

The pleura normally contains 4.1-12.7 mL of fluid.¹ Pathological conditions can disrupt the homeostasis of formation and absorption of pleural fluid, thereby causing pleural effusion. The identification of fluid as exudative or transudative is the most essential step in ruling out the cause of pleural effusion. Congestive heart failure, Nephrotic Syndrome and Hepatic Cirrhosis are among the common causes of transudative pleural effusion while Tuberculosis, Parapneumonic effusion, Primary and metastatic lung cancer, Vasculitis and Pancreatitis are often listed under exudative pleural effusion which are often local cause.²

Differentiation of pleural effusion on the basis of clinical and radiological finding is incompetent. An additional biochemical work up is done, whereby protein content and LDH in serum and pleural fluid is analyzed to differentiate transudative and exudative types of pleural effusion, which is the basis of Light's criteria.³ Several other biochemical parameters have been evaluated for differentiation of exudative from transudative type like pleural fluid to serum cholesterol ratio, pleural fluid to serum cholinesterase ratio⁶, pleural fluid to serum bilirubin level, pleural fluid pH and glucose level.⁴⁻⁹ Most of these results require 1 or 2 working days and are less specific. Therefore, a drop hydrogen peroxide test is done which is shown to have sensitivity and specificity comparable to Light's criteria along with reduction in pre-analytical error when performed in bedside.^{10,11}

METHODS

A concurrent validity test was done in the Department of Internal Medicine of Dhulikhel Hospital from January to September, 2021. Convenient sampling method was used and data were collected from 83 participants. All the patients who had clinical and radiological evidence of pleural effusion, who had not been previously evaluated were included in the study. Diagnostic thoracentesis was performed under the aseptic precautions and 10 ml fluid was withdrawn. Two milliliters of tapped fluid was collected in a test tube, where one to two drops of 20% hydrogen peroxide was added. After a few seconds of gentle shaking of the tube, the presence of visible air bubbles in the tube was observed. Presence of profuse bubbles was taken as exudative fluid (fig. 1) and its absence as transudative type (fig. 2). One sample was sent for pleural fluid protein and LDH level along with blood sample for serum protein and LDH to determine Light's criteria. Validity of the drop peroxide test was compared with the Light's criteria. The study was conducted after receiving ethical approval from the Institutional Review Committee (IRC) of KUSMS, Dhulikhel Hospital and informed expressed consent was taken from all patients.



Figure 1. Exudative pleural effusion showing presence of air bubbles

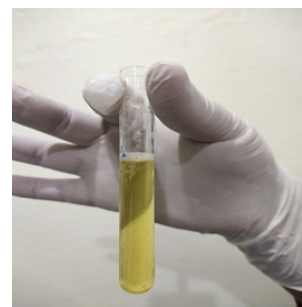


Figure 2. Transudative pleural effusion with no bubble formation

Data was collected and entered into Microsoft Excel. Descriptive statistics including mean, median, frequency and percentage were done. Sensitivity and specificity, and positive and negative predictive value of drop hydrogen peroxide test were done to assess the validity.

RESULTS

A total of 83 patients who were newly diagnosed with a case of pleural effusion based on clinical and radiological grounds were included in the study. There were 50 males and 33 female patients. The mean age of the participants was 53.2 ± 20.7 years. A total of 43 patients had transudative pleural effusion while 40 patients had exudative pleural effusion based on Light's criteria. Similarly, 37 patients had transudative pleural effusion while 46 patients had exudative pleural effusion based on drop hydrogen peroxide test (Table 1). Results discrepancies were noticed in nine subjects.

Table 1. Type of pleural fluid based on Light's criteria and drop hydrogen peroxide test

		Light's criteria		Total
		Exudative	Transudative	
Drop Hydrogen Peroxide Test	Exudative	34	3	37
	Transudative	6	40	46
		40	43	83

For statistical analysis, true positives were considered when both tests revealed exudation. True negatives were considered when both tests revealed transudative. Hence, the number of True positives was 34 and the number of true negatives was 40. Three samples were false positive, that is exudative by drop hydrogen peroxide test but transudative by Light's criteria and six samples were false negative, that is transudative by drop hydrogen peroxide test but exudative by Light's criteria.

Above outcomes derives following inferences:

The sensitivity and specificity of drop hydrogen peroxide test is 85% and 93% respectively, PPV (Positive predictive

value) of 91.9% and NPV (Negative predictive value) of 87%. The diagnostic accuracy of the drop hydrogen peroxide test is 89.15%.

DISCUSSION

Proper history taking and physical examination are critical in diagnosing a case of pleural effusion, followed by a chest radiography. Chest radiography (Posteroanterior and lateral view) usually confirms the presence of a pleural effusion. Furthermore, thoracentesis is done under aseptic conditions and the pleural fluid thus tapped is used. Pleural effusions are either transudates or exudates based on the biochemical characteristics of the fluid, which usually reflect the physiologic mechanism of its formation. Thus, the next step is to evaluate the nature of pleural fluid and narrow down the differential diagnosis.

Additionally, if direct diagnosis of pleural effusion cannot be found via analysis of the fluid appearance and biochemical parameters, further radiological investigations like CT or invasive procedures like pleural biopsy can be done.¹¹

In recent years, the need for prompt diagnosis and treatment in some cases of pleural effusion has led to formulation of several bedside tests which are cheap as well as readily available. Some of which include analysis of pleural pH, pleural glucose and drop hydrogen peroxide test. Despite these attempts in strengthening specificity of Light's criteria, most centers still continue to use Light's criteria to differentiate exudate and transudate, which leaves this interpretation unequivocal.¹²

Our study is based on a principle that exudative pleural fluid has high catalase activity.¹¹ Addition of hydrogen peroxide compound in this fluid gets cleaved by the catalase enzyme and liberates oxygen forming visible bubbles and water, giving an instant impression of the type of fluid.

Our study, which measured the concurrent validity of drop hydrogen peroxide test against standard Light's criteria in 83 subjects, showed the sensitivity and specificity of this test as 85% and 93% respectively, PPV of 91.9% and NPV of 87% slightly more compared to Taksande et al.¹¹ The diagnostic accuracy of the drop hydrogen peroxide test in our study is 89.15% to differentiate the nature of pleural fluid into exudative and transudative.

Taksande et al. conducted similar study with sample size of 172, where the sensitivity and specificity of A drop hydrogen peroxide test was 80.7% and 81.8% respectively, whereas PPV (Positive predictive value) was 96.8% and NPV (Negative predictive value) was 38.3%.¹¹ According to their study, there might have been more exudative pleural effusion because of inclusion of blood mixed samples as well.

The study conducted by Sarkar et al. with sample size of 52, showed that all exudative pleural fluids showed bubbling in addition to Hydrogen Peroxide, whereas none of the transudative pleural fluids showed bubbling.¹⁰ However, in their study, when catalase or blood was added to transudative pleural fluid, bubbling was observed following addition of Hydrogen Peroxide. They concluded that blood uncontaminated pleural fluid can be differentiated into exudative and transudative easily in bedside within a short period of time with sensitivity and specificity comparable to Light's criteria.

CONCLUSION

Evaluation of pleural fluid using a drop hydrogen peroxide allows prompt bedside differentiation of pleural effusion into transudative or exudative type. In contrast to frequently abided diagnostic evaluation by Light's criteria which takes about 1 or 2 working days, this test gives quick results. This rapid differentiation is advantageous especially in critically ill patients, who require timely clinical management and therapeutic intervention. Moreover, the affordability of the test makes the test patient friendly in settings with a greater number of indigent population and limited laboratory facilities. To increase the validity, additional tests can be incorporated which increases the specificity and diagnostic accuracy of the test. These tests will aid in identifying the cause of the effusion once the exudative or transudative nature has been verified by the Hydrogen Peroxide test. For example, differential leukocyte count can be used to narrow down the differentials, amylase concentration can be used to rule out concurrent acute pancreatitis, pleural fluid pH can be measured to rule out suspected infectious etiology in non-purulent pleural effusion. All and all implication of this test which has similar sensitivity and specificity to Light's criteria, especially in resource limited countries like Nepal, will help the patients financially and clinicians to reach a diagnosis promptly.

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